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07/715,397	06/14/91	COCHRANE	C [illegible]

EXAMINER: PERKINS, G

ART UNIT	PAPER NUMBER
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THE SCRIPPS RESEARCH INSTITUTE
OFFICE OF PATENT COUNSEL
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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

514/369 514/12

☐ This application has been examined ☑ Responsive to communication filed on 4-15-92 & 6-22-92 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☑ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☑ Notice of Art Cited by Applicant, PTO-1449. (2 sheets)
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 1-8 are pending in the application.
   Of the above, claims ——— are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☑ Claims 1-8 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 9-89)

15. The text of those sections of 35 U.S. Code not included in this action can be found in a previous Office action.

16. Claims 1-8 are pending in this application. Claim 1 has been amended as requested by applicant in the communication filed April 15, 1992. Claims 6-8 have been added as requested in the same communication.

For purposes of clarification of the record and for purposes of application of prior art, the examiner will go through each claim, stating whether or not the claim is supported by adequate written description by the instant specification, and what filing date applies to the claimed subject matter. Applicant is directed to MPEP 201.11 "When Not Entitled To Benefit Of Filing Date". Starting first with the new claims, claims 6-8:

It is noted that new claim 6 is fully supported by the instant application. The subject matter of claim 6 however was not adequately described by the parent application Serial No. 07/293,201. The peptide, $(KL_4)_4$ was first introduced and adequately described in this C-I-P application. While the earlier application describes a genus which includes $(KL_4)_4$, a genus is not adequate written description for a species within it unless the genus is extremely small (which is not the case here). Accordingly, claim 6 has the filing date of this C-I-P application, June 14, 1991 for purposes of prior art, etc..

It is noted that as to new claim 7, there is support for the new ranges of "a", "b", "c" at page 27 (as pointed out in the Response) and support for "d" at page 6, line 3. At page 6 "d" is described as having a value of "0 to 3, and is preferably 1". The

description of the newly claimed range for "d" in new claim 7, that is "d is 0 to 2", is fully supported at page 6, line 19 and is therefor not deemed new matter to the claimed subject matter. It is noted however that the parent application, Serial No. 07/293, 201, describes "d" in the same manner as found at page 27 of this specification, that is "d" is described as being "1 to 3, preferably 1 to 2" (see page 29 of the parent application). There is no written description in the parent application that "d" can be 0. On this basis, claim 7 contains new matter between the parent application and the instant application. Claim 7 is therefor not entitled to benefit from the effective filing date of the 07/293, 201 application. Claim 7 is entitled only to this C-I-P actual filing date of June 14, 1991.

As to claim 8, claim 8 is fully supported by the instant application but it also contains claimed features which are newly described in the instant application, namely the last 3 peptide species listed in claim 8, which were not adequately described in the parent application. A genus is not adequate written description for a species within it. Since claim 8 contains a new feature, i.e. three new peptides, it is entitled only to the June 14, 1991, C-I-P filing date. See MPEP 201.11.

Newly amended claim 1 is fully supported by the instant application and the earlier filed applications. It is noted, as pointed out by applicant, the amendment to "linear" polypeptides is supported at page 11, lines 3-8. The amendment is especially supported by page 11, line 5; "linear series of no more than 60 amino acid residues". The amendment is further supported by the preferred embodiments, all of which are linear. See especially Table 3. The earlier applications also described these same linear

peptides and therefore claim 1 benefits from the filing date of the grandparent application, January 6, 1988.

Concerning original claims 2-5:

Claims 2, 4, and 5, for reasons similar to those set out above with regard to claims 6 and 8, because they contain peptide species which were first introduced and supported by this application they are entitled only to the filing date of this application.

Claim 3, similar to claim 1, is adequately supported in the earlier applications and is entitled to the benefit of the effective filing date of the grandparent application.

17. Applicant has complied with the Sequence Rules to the extent of filing a Sequence Listing and a computer readable form of the Listing. Applicant is however still advised to review and amend the specification and claims as necessary to comply with Rule 1.821(d); "reference must be made to the sequence by use of the assigned identifier, in the text of the description or claims...". Claim 8 for example does not give the Seq. ID Numbers for the last three species listed.

18. The rejection of claims 1-5 under 35 U.S.C. §112, first paragraph (i.e. lack of enablement) is withdrawn. Applicant's persuasive arguments, in combination with the two Declarations by Dr. Cochrane and Ms. Revak, which provide ample evidence regarding

the use of the claimed invention, are sufficient to remove the basis of the instant rejection.

19. The rejection of claim 1 under 35 U.S.C. §102(a) or (b) as anticipated by, or in the alternative, §103 as being obvious over Ono et al. is withdrawn. Though the examiner cannot agree with applicant's analysis regarding inherency and what the reference must teach when it is clear that the compound disclosed in the art is structurally the same or similar to the claimed compound, the examiner does agree with applicant that this rejection does not apply to the claims as amended. On the basis of the amended claims, which clearly claim only linear polypeptides, the rejection is removed. It is noted, as pointed out by applicant, the amendment to "linear" polypeptides is supported at page 11, lines 3-8. The amendment is especially supported by page 11, line 5; "linear series of no more than 60 amino acid residues". The amendment is further supported by the preferred embodiments, all of which are linear. See especially Table 3.

20. The rejection of claims 1 and 3 under 35 U.S.C. §103 as being unpatentable over Jackson is maintained. This rejection is maintained for essentially the same reasons as the rejection of claims 1 and 3 under this statutory provision and in light of this art, as set forth in paragraph 19 of the September 30, 1991 Office action. Applicant's arguments, filed April 15, 1992, have been fully considered but they are not deemed to be persuasive.

Applicant contends that a §103 rejection must be based on a combination of two or more references and argues that this §103

rejection must therefore be in error since it is only based on a single reference to Jackson. A single reference may render obvious a claimed invention. Such is often the case when the reference discloses a genus and applicant claims a species (either explicitly or within a claimed generic formula) falling within that disclosed genus. A generic disclosure suggests prima facie obvious a species within it; *Merck v. Biocraft,* 10 USPQ 2d, 1843 (Fed. Cir. 1989) (prior art patent which teaches a genus of 1,200 combinations renders obvious one single combination even though prior art does not highlight this combination), *In re Susi,* 169 USPQ 423 (CCPA 1971) (obviousness rejection affirmed where the disclosure of the prior art was "huge" but it undeniably included at least some of the compounds recited in appellant's generic claims").

As discussed in a telephonic interview with April Logan on August 5th and August 7th, it was agreed that at least one peptide specie fell within Jackson's generic formula which is also embraced by the instant generic of claims 1 and 3. Such is the case since, as pointed out in the parent application, nearly any residue can be "Tyr" (one of Applicant's "U" amino acids). There is a reasonable expectation of success from the Jackson patent that <u>any</u> of the peptides which are embraced by the generic formula taught therein would be polypeptides useful in the treatment of RDS.

Applicant may obviate the Jackson patent as prior art by deleting "Y" as being one of the possible amino acid substitutions for applicant's U variable. Deletion of tyrosine from the claims would obviate any overlap in species between the Jackson generic and the instant generic claims. Applicant is encouraged to delete "Y" in claims 1 and 3. Such will overcome this §103 rejection and such a deletion from the generic formula is NOT considered to be new matter. The new subgenus without "Y" would be adequately supported

by the generic as it stands and would be further supported by the fact none of the preferred species have tyrosine residues within them. The deletion of "Y" would meet the standard set forth in In re Smith and here the description is close enough to comply with §112 ("precisely how close the description must come to comply with §112 must be left to case-by case development", In re Smith, 173 USPQ 679, 683).

21. The provisional rejection of claims 1, 3, 7, and 8 under the judicially created doctrine of double patenting as being unpatentable over claims 18 and 35-39 of copending application Serial No. 07/293,201 is maintained. This provisional rejection is maintained for essentially the same reason as the provisional rejection of claims 1-5 under this judicial doctrine as set forth in paragraph 20 of the September 30, 1991 Office action. Applicant's arguments, filed April 15, 1992, have been fully considered but they are not deemed to be persuasive.

Applicant argues at page 14 of the Response that applicant respectfully disagrees with this provisional rejection. However since applicant presents no reasons as to why applicant disagrees, such arguments cannot be deemed persuasive.

Applicant has set forth that applicant is willing to file a Terminal Disclaimer. Applicant must file a Disclaimer to obviate the basis of this rejection since the 07/293,201 application has already been Allowed. As set forth in the prior Office action, some of the instant claims overlap in scope with those of the '201 application. For example claims 1, 3, and 7, embrace the preferred polypeptide species that have already been allowed in the parent application. It would be an unconstitutional extension of applicant's exclusionary

interest as to these preferred species to issue one patent claiming these species and then at a later time issue a second patent which claims also cover these same species by virtue of a generic claim. This would extend applicant's exclusionary interest as to these particular peptides beyond seventeen years. Moreover, new claim 8 clearly claims some of the same peptides (e.g. $(RL_4)_4$).

22. Claims 2, 4, 5, 6, 7, and 8 are rejected under 35 U.S.C. 103 as being unpatentable over Cochrane (WO89/06657; July 27 1989).

For the reasons set forth in paragraph 16 of this Office action, claims 2, and 4-8 are entitled only to the filing date of this C-I-P application, June 14, 1991. Each of these claims contain matter first introduced and supported by this application and none of these claims are entitled to benefit from the filing date of the earlier filed applications for the reasons set forth above. See also MPEP 201.11.

On this basis the PCT publication by Cochrane et al. is prior art to this application. This prior art reference makes obvious the instant claimed peptides which replace Arg with Lys. See for example Table 3 on page 30 which discloses DL4 and RL4 peptides and page 29 discloses that R (Arg) or D (Asp) may be substituted with K (Lys). See especially line 4 of page 29. Cochrane et al. teaches that KL4 and other KCL peptides similar to those of the RL and RCL peptides are obvious variants of RL and RCL peptides disclosed.

Applicant may obviate this obviousness rejection by showing that the KL peptides are unexpectedly superior to the RL peptides of the prior art. A direct comparison of, for example $(RL_4)_4$ and (KL4)4, in an *in vitro* surfactant assay, which show the KL4 peptides

to be unexpectedly superior to the RL4 peptides would overcome this rejection since the Cochrane disclosure would lead one to expect the peptides with Lys would have the same or similar activity as those with Arg. The disclosure does not suggest that they would be better than the peptides with Arg. *In vitro* data would be sufficient since the in vitro data can be extrapolated to *in vivo* utility, as evidenced by the monkey data and other evidence provided in the two Declarations.

23. Claims 2, 4, 5, 6, 7, and 8 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 18 and 35-39 of copending application Serial No. 07/293,102 in view of Cochrane et al. (WO89/06657).

Cochrane et al. makes obvious the Lys containing peptides as discussed in the preceding paragraph. It would be obvious to substitute the Arg residue in the peptides of claims 18 and 35-39 of the copending application with Lys based on the Cochrane et al. disclosure which teaches that such substitutions of Lys for Arg should result in peptides having similar surfactant activity. See page 29 of Cochrane et al.. In the absence of unexpected superiority, these claims are provisionally rejected as being obvious over the other Allowed claims in light of Cochrane et al..

This is a provisional obviousness-type double patenting rejection.

24. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

"A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States."

25. Claims 7 and 8 are rejected under 35 U.S.C. § 102 (b) as being clearly anticipated by Cochrane et al. (WO89/06657).

Claims 7 and 8 are only entitled to the filing date of the instant application for the reasons discussed in paragraph 16 of this Office action. Cochrane et al. discloses peptides with phospholipid which are peptides of the pulmonary surfactants of claims 7 and 8. See especially page 30 of Cochrane et al. For example the RL4 surfactant polypeptide, which is taught in Table 3 of Cochrane et al. is also embraced by instant claims 7 and 8. The prior art need only disclose one species falling with a claimed genus to anticipate said genus. *Titanium Metals Corp. v. Banner*, 227 USPQ 773 (CAFC 1985). Cochrane et al. discloses several of the same compositions as embraced by the rejected claims. Any showing of unexpectedly superiority to obviate the §103 rejection in light of Cochrane will not obviate this §102 rejection since the rejected claims embrace surfactants which are clearly taught by the prior art and which clearly anticipate the instant claims. See *Titanium Metals*; "without novelty evidence of unobviousness is superfluous". Claims 7 and 8 lack novelty on the basis Cochrane specifically

disclosing preferred peptides which are embraced by instant claims 7 and 8.

26. In sum, it should be noted that claims 1 and 3 would be allowable with a deletion of "Y" as a substition for the U variable and with the filing of a Terminal Disclaimer.

27. The art cited but not relied upon (Revak et al.) id deemed to be related to the nature of this application. Revak et al. does not teach or suggest peptides of the instant invention.

It is noted that applicant has sent many of the same references accompanying the PTO-1449 (Information Disclosure Statement, IDS) that had already been officially made of record by way of the PTO-892 forms which were mailed with two prior Office actions (e.g. Jackson, Segrest, Kaiser, Enhoring, etc.). Applicant need not resubmit references in an IDS which have already been considered and made of record by the examiner as evidenced by a PTO-892 form.

28. No claims are allowed.

29. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Susan Perkins whose telephone number is (703)-308-1030. Any inquiry of a general nature or relating to the status of this application

should be directed to the Group receptionist whose telephone number is (703)-308-0196.

S.M.Perkins
August 09, 1992

MERRELL C. CASHION, JR.
SUPERVISORY PATENT EXAMINER
GROUP 180